electron density map of the structure whose coordinates are unknown. This, in turn, can be subjected to any well-known model building and structure refinement techniques to provide a final, accurate structure of the unknown crystallized molecule or molecular complex (Lattman, "Use of the Rotation and Translation Functions," in Meth. Enzymol. 115, pp. 55-77 (1985); M.G. Rossman, ed., The Molecular Replacement Method - A Collection of Papers on the Use of Non-Crystallographic Symmetry, Intl. Sci. Rev. Ser. No. 13, Gordon & Breach, New York (1972)).

B1 cont

Please replace the paragraph at page 28, lines 9-17, with the following rewritten paragraph. Per 37 C.F.R §1.121, this paragraph is also shown in Appendix A, page A2, with notations to indicate the changes made.

Useful programs to aid one of skill in the art in connecting the individual chemical entities or fragments include, without limitation, CAVEAT (Bartlett et al., in "Molecular Recognition: Chemical and Biological Problems," Special Publ., Royal Chem. Soc., 78:182-96 (1989); Lauri et al., J. Comput. Aided Mol. Des. 8:51-66 (1994); available from the University of California, Berkeley, CA);

B2

3D database systems such as ISIS (available from MDL Information Systems, San Leandro, CA; reviewed in Martin, J. Med. Chem. 35:2145-54 (1992)); and HOOK (Eisen et al., Proteins: Struc., Funct., Genet. 19:199-221 (1994); available from Molecular Simulations, San Diego, CA).

Please replace the paragraph at page 28, lines 18-26, with the following rewritten paragraph. Per 37 C.F.R §1.121, this paragraph is also shown in Appendix A, page A2, with notations to indicate the changes made.

Human beta secretase binding compounds may be designed "*de novo*" using either an empty binding site or optionally including some portion(s) of a known inhibitor(s). There are many *de novo* ligand design methods including, without limitation, LUDI (Böhm, J. Comp. Aid. Molec. Design. 6:61-78 (1992); B3 available from Molecular Simulations Inc., San Diego, CA); LEGEND (Nishibata et al., Tetrahedron, 47:8985 (1991); available from Molecular Simulations Inc., San Diego, CA); LeapFrog (available from Tripos Associates, St. Louis, MO); and SPROUT (Gillet et al., J. Comput. Aided Mol. Design 7:127-53 (1993); available from the University of Leeds, UK).